Exhibit B.pdf

<!--StartFragment-->RESULT 2
MCTS1_HUMAN
ID   MCTS1_HUMAN   Reviewed;   181 AA.
AC   Q9ULC4; Q502X6;
DT   22-JUL-2008, integrated into UniProtKB/Swiss-Prot.
DT   01-MAY-2000, sequence version 1.
DT   16-DEC-2008, entry version 58.
DE   RecName: Full=Malignant T cell amplified sequence 1;
DE   Short=MCT-1;
DE   AltName: Full=Multiple copies T-cell malignancies;
GN   Name=MCTS1; Synonyms=MCT1;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
OC   Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1), FUNCTION, AND TISSUE
RP   SPECIFICITY.
RX   MEDLINE=98438033; PubMed=9766643;
RA   Prosniak M., Dierov J., Okami K., Tilton B., Jameson B., Sawaya B.E.,
RA   Gartenhaus R.B.;
RT   "A novel candidate oncogene, MCT-1, is involved in cell cycle
RT   progression.";
RL   Cancer Res. 58:4233-4237(1998).
RN   [2]
RP   NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1).
RX   PubMed=16533400; DOI=10.1186/1471-2164-7-48;
RA   Kemmer D., Podowski R.M., Arenillas D., Lim J., Hodges E., Roth P.,
RA   Sonnhammer E.L.L., Hoeoeg C., Wasserman W.W.;
RT   "NovelFam3000 -- uncharacterized human protein domains conserved
RT   across model organisms.";
RL   BMC Genomics 7:48-48(2006).
RN   [3]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 1).
RX   PubMed=14702039; DOI=10.1038/ng1285;
RA   Ota T., Suzuki Y., Nishikawa T., Otsuki T., Sugiyama T., Irie R.,
RA   Wakamatsu A., Hayashi K., Sato H., Nagai K., Kimura K., Makita H.,
RA   Sekine M., Obayashi M., Nishi T., Shibahara T., Tanaka T., Ishii S.,
RA   Yamamoto J., Saito K., Kawai Y., Isono Y., Nakamura Y., Nagahari K.,
RA   Murakami K., Yasuda T., Iwayanagi T., Wagatsuma M., Shiratori A.,
RA   Sudo H., Hosoiri T., Kaku Y., Kodaira H., Kondo H., Sugawara M.,
RA   Takahashi M., Kanda K., Yokoi T., Furuya T., Kikkawa E., Omura Y.,
RA   Abe K., Kamihara K., Katsuta N., Sato K., Tanikawa M., Yamazaki M.,
RA   Ninomiya K., Ishibashi T., Yamashita H., Murakawa K., Fujimori K.,
RA   Tanai H., Kimata M., Watanabe M., Hiraoka S., Chiba Y., Ishida S.,
RA   Ono Y., Takiguchi S., Watanabe S., Yosida M., Hotuta T., Kusano J.,
RA   Kanehori K., Takahashi-Fujii A., Hara H., Tanase T.-O., Nomura Y.,
RA   Togiya S., Komai F., Hara R., Takeuchi K., Arita M., Imose N.,
RA   Musashino K., Yuuki H., Oshima A., Sasaki N., Aotsuka S.,
RA   Yoshikawa Y., Matsunawa H., Ichihara T., Shiohata N., Sano S.,
RA   Moriya S., Momiyama H., Satoh N., Takami S., Terashima Y., Suzuki O.,
RA   Nakagawa S., Senoh A., Mizoguchi H., Goto Y., Shimizu F., Wakebe H.,
RA   Hishigaki H., Watanabe T., Sugiyama A., Takemoto M., Kawakami B.,
RA   Yamazaki M., Watanabe K., Kumagai A., Itakura S., Fukuzumi Y.,
RA   Fujimori Y., Komiyama M., Tashiro H., Tanigami A., Fujiwara T.,
RA   Ono T., Yamada K., Fujii Y., Ozaki K., Hirao M., Ohmori Y.,
RA   Kawabata A., Hikiji T., Kobatake N., Inagaki H., Ikema Y., Okamoto S.,
RA   Okitani R., Kawakami T., Noguchi S., Itoh T., Shigeta K., Senba T.,
RA   Matsumura K., Nakajima Y., Mizuno T., Morinaga M., Sasaki M.,
RA   Togashi T., Oyama M., Hata H., Watanabe M., Komatsu T.,

RA Mizushima-Sugano J., Satoh T., Shirai Y., Takahashi Y., Nakagawa K.,
RA Okumura K., Nagase T., Nomura N., Kikuchi H., Masuho Y., Yamashita R.,
RA Nakai K., Yada T., Nakamura Y., Ohara O., Isogai T., Sugano S.;
RT "Complete sequencing and characterization of 21,243 full-length human
RT cDNAs.";
RL Nat. Genet. 36:40-45(2004).
RN [4]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RA Mural R.J., Istrail S., Sutton G.G., Florea L., Halpern A.L.,
RA Mobarry C.M., Lippert R., Walenz B., Shatkay H., Dew I., Miller J.R.,
RA Flanigan M.J., Edwards N.J., Bolanos R., Fasulo D., Halldorsson B.V.,
RA Hannenhalli S., Turner R., Yooseph S., Lu F., Nusskern D.R.,
RA Shue B.C., Zheng X.H., Zhong F., Delcher A.L., Huson D.H.,
RA Kravitz S.A., Mouchard L., Reinert K., Remington K.A., Clark A.G.,
RA Waterman M.S., Eichler E.E., Adams M.D., Hunkapiller M.W., Myers E.W.,
RA Venter J.C.;
RL Submitted (SEP-2005) to the EMBL/GenBank/DDBJ databases.
RN [5]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORMS 1 AND 2).
RC TISSUE=Chondrosarcoma, and Eye;
RX PubMed=15489334; DOI=10.1101/gr.2596504;
RG The MGC Project Team;
RT "The status, quality, and expansion of the NIH full-length cDNA
RT project: the Mammalian Gene Collection (MGC).";
RL Genome Res. 14:2121-2127(2004).
RN [6]
RP FUNCTION.
RX PubMed=10440924;
RX DOI=10.1002/(SICI)1097-4644(19990915)74:4<544::AID-JCB4>3.3.CO;2-W;
RA Dierov J., Prosniak M., Gallia G., Gartenhaus R.B.;
RT "Increased G1 cyclin/cdk activity in cells overexpressing the
RT candidate oncogene, MCT-1.";
RL J. Cell. Biochem. 74:544-550(1999).
RN [7]
RP FUNCTION, SUBCELLULAR LOCATION, AND INDUCTION.
RX PubMed=11709712; DOI=10.1038/sj.onc.1204881;
RA Herbert G.B., Shi B., Gartenhaus R.B.;
RT "Expression and stabilization of the MCT-1 protein by DNA damaging
RT agents.";
RL Oncogene 20:6777-6783(2001).
RN [8]
RP FUNCTION.
RX PubMed=12637315; DOI=10.1182/blood-2002-11-3486;
RA Shi B., Hsu H.-L., Evens A.M., Gordon L.I., Gartenhaus R.B.;
RT "Expression of the candidate MCT-1 oncogene in B- and T-cell lymphoid
RT malignancies.";
RL Blood 102:297-302(2003).
RN [9]
RP FUNCTION.
RX PubMed=16322206; DOI=10.1158/0008-5472.CAN-05-0845;
RA Levenson A.S., Thurn K.E., Simons L.A., Veliceasa D., Jarrett J.,
RA Osipo C., Jordan V.C., Volpert O.V., Satcher R.L. Jr.,
RA Gartenhaus R.B.;
RT "MCT-1 oncogene contributes to increased in vivo tumorigenicity of
RT MCF7 cells by promotion of angiogenesis and inhibition of apoptosis.";
RL Cancer Res. 65:10651-10656(2005).
RN [10]
RP FUNCTION.
RX PubMed=15897892; DOI=10.1038/sj.onc.1208680;
RA Hsu H.-L., Shi B., Gartenhaus R.B.;
RT "The MCT-1 oncogene product impairs cell cycle checkpoint control and

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RT   transforms human mammary epithelial cells.";
RL   Oncogene 24:4956-4964(2005).
RN   [11]
RP   FUNCTION, SUBCELLULAR LOCATION, PUA DOMAIN, AND INTERACTION WITH DENR.
RX   PubMed=16982740; DOI=10.1158/0008-5472.CAN-06-1999;
RA   Reinert L.S., Shi B., Nandi S., Mazan-Mamczarz K., Vitolo M.,
RA   Bachman K.E., He H., Gartenhaus R.B.;
RT   "MCT-1 protein interacts with the cap complex and modulates messenger
RT   RNA translational profiles.";
RL   Cancer Res. 66:8994-9001(2006).
RN   [12]
RP   FUNCTION.
RX   PubMed=17416211; DOI=10.1016/j.dnarep.2007.02.028;
RA   Hsu H.-L., Choy C.O., Kasiappan R., Shih H.-J., Sawyer J.R.,
RA   Shu C.-L., Chu K.-L., Chen Y.-R., Hsu H.-F., Gartenhaus R.B.;
RT   "MCT-1 oncogene downregulates p53 and destabilizes genome structure in
RT   the response to DNA double-strand damage.";
RL   DNA Repair 6:1319-1332(2007).
RN   [13]
RP   FUNCTION, PHOSPHORYLATION, AND MUTAGENESIS OF THR-81 AND SER-118.
RX   PubMed=17016429; DOI=10.1038/sj.onc.1210030;
RA   Nandi S., Reinert L.S., Hachem A., Mazan-Mamczarz K., Hagner P.,
RA   He H., Gartenhaus R.B.;
RT   "Phosphorylation of MCT-1 by p44/42 MAPK is required for its
RT   stabilization in response to DNA damage.";
RL   Oncogene 26:2283-2289(2007).
CC   -!- FUNCTION: Anti-oncogene that play a role in cell cycle regulation;
CC       decreases cell doubling time and anchorage-dependent growth;
CC       shortens the duration of G1 transit time and G1/S transition. When
CC       constituvely expressed, increases CDK4 and CDK6 kinases activity
CC       and CCND1/cyclin D1 protein level, as well as G1 cyclin/CDK
CC       complex formation. Plays a role as translation enhancer; Recruits
CC       the density-regulated protein/DENR and binds to the cap complex of
CC       the 5'-terminus of mRNAs, subsequently altering the mRNA
CC       translation profile; Up-regulates protein levels of BCL2L2, TFDP1,
CC       MRE11A, CCND1 and E2F1, while mRNA levels remains constant.
CC       Hyperactivates DNA damage signaling pathway; increased gamma-
CC       irradiation-induced phosphorylation of histone H2AX, and induces
CC       damage foci formation. Increases the overall number of chromosomal
CC       abnormalities such as larger chromosomes formation and multiples
CC       chromosomal fusions when over-expressed in gamma-irradiated cells.
CC       May play a role in promoting lymphoid tumor development: lymphoid
CC       cell lines over-expressing MCTS1 exhibit increased growth rates
CC       and display increased protection against apoptosis. May contribute
CC       to the pathogenesis and progression of breast cancer via promotion
CC       of angiogenesis through the decline of inhibitory
CC       THBS1/thrombospondin-1, and inhibition of apoptosis. Involved in
CC       the process of proteosome degradation to down-regulate Tumor
CC       suppressor p53/TP53 in breast cancer cell; Positively regulates
CC       phosphorylation of MAPK1 and MAPK3.
CC   -!- SUBUNIT: Interacts (via PUA domain) with DENR.
CC   -!- SUBCELLULAR LOCATION: Cytoplasm. Note=Nuclear relocalization after
CC       DNA damage.
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC       Name=1;
CC         IsoId=Q9ULC4-1; Sequence=Displayed;
CC       Name=2;
CC         IsoId=Q9ULC4-2; Sequence=VSP_034856;
CC   -!- TISSUE SPECIFICITY: Ubiquitous. Over-expressed in T-cell lymphoid
CC       cell lines and in non-Hodgkin lymphoma cell lines as well as in a
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CC       subset of primary large B-cell lymphomas.
CC   -!- INDUCTION: By DNA damaging agents such as gamma irradiation,
CC       adriamycin or taxol in lymphoid cells, but not by stress stimuli
CC       such as heat shock. This induction of protein expression does not
CC       occur at the RNA level, and does not require new protein
CC       synthesis.
CC   -!- DOMAIN: The PUA RNA-binding domain is critical for cap binding,
CC       but not sufficient for translation enhancer function. MCT1 N-
CC       terminal region is required to enhance translation possibly trough
CC       interaction with other proteins.
CC   -!- PTM: Phosphorylation is critical for stabilization and promotion
CC       of cell proliferation.
CC   -!- SIMILARITY: Belongs to the MCTS1 family.
CC   -!- SIMILARITY: Contains 1 PUA domain.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; AB034206; BAA86055.1; -; mRNA.

  Query Match             100.0%;  Score 181;  DB 1;  Length 181;
  Best Local Similarity   100.0%;  Pred. No. 3.6e-184;
  Matches  181;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MFKKFDEKENVSNCIQLKTSVIKGIKNQLIEQFPGIEPWLNQIMPKKDPVKIVRCHEHIE 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MFKKFDEKENVSNCIQLKTSVIKGIKNQLIEQFPGIEPWLNQIMPKKDPVKIVRCHEHIE 60

Qy         61 ILTVNGELLFFRQREGPFYPTLRLLHKYPFILPHQQVDKGAIKFVLSGANIMCPGLTSPG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 ILTVNGELLFFRQREGPFYPTLRLLHKYPFILPHQQVDKGAIKFVLSGANIMCPGLTSPG 120

Qy        121 AKLYPAAVDTIVAIMAEGKQHALCVGVMKMSAEDIEKVNKGIGIENIHYLNDGLWHMKTY 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 AKLYPAAVDTIVAIMAEGKQHALCVGVMKMSAEDIEKVNKGIGIENIHYLNDGLWHMKTY 180

Qy        181 K 181
              |
Db        181 K 181
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